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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,481	05/15/2008	Zissimos Mourclatos	130694.02801	6145
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Pepper Hamilton LLP 400 Berwyn Park 899 Cassatt Road Berwyn, PA 19312-1183			EXAMINER SHIN, DANA H	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 06/25/2010	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/576,481

**Applicant(s)**

MOURELATOS ET AL.

**Examiner**

DANA SHIN

**Art Unit**

1635

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 April 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5, 10, 13, 39, 48-50 and 52 is/are pending in the application.
- 4a) Of the above claim(s) 39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 10, 13, 48-50 and 52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB06)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of Application/Amendment/Claims***

This Office action is in response to the communications filed on April 13, 2010.

Currently, claims 1-5, 10, 13, 39, 48-50, and 52 are pending. Note that claim 39 is a withdrawn from further consideration as being drawn to a non-elected invention. Note that claim 39 belongs to Group V, whereas applicant has elected Group I for examination. See the restriction requirement dated July 6, 2009 and the election reply filed on August 6, 2009. Claim 39 was inadvertently included in the "rejected" claims on PTOL-326 mailed on November 13, 2009, which is why the Office action dated November 13, 2009 did not include claim 39 in any of the rejections, priority denial, and claim objections. Again, claim 39 was not considered or examined in the last Office action as it was drawn to a non-elected invention. Accordingly, claims 1-5, 10, 13, 48-50, and 52 are currently under examination on the merits in the instant case.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Response to Arguments and Amendments***

#### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

**Maintained Objections/Rejections**

***Priority***

The denial of granting the 60/513,489 priority date for claims 1-5, 10, 13, 48-50, and 52 remains effective for the reasons of record as set forth in the Office action mailed on November 13, 2009 and for the reasons stated below.

Applicant argues that page 7, last sentence of 60/513,489 provides adequate written description support for the claimed methods. Contrary to applicant's argument, the one sentence does not provide adequate written description support for the claimed methods because it fails to describe the necessary method steps claimed in the instant case. Applicant has further pointed out Figure 4 for the alleged written description support. However, neither Figure 4A nor Figure 4B adequately describes all of the method steps claimed in the instant case. At best, the drawings in Figures 4A-4B depict that "only a portion of an miRNA, bound to an Argonaute protein, is required for target RNA recognition and cleavage (summarized in a schematic form in Figure 4)." and that "critical determinant of siRNA specificity (as defined in this study) are the nucleotides shown in Figure 4." See page 7 of the 60/513,489 specification. There is nothing whatsoever in page 7 or Figure 4 that provides adequate written description for the claimed uniquely targeting siRNA nucleotide sequence identification methods comprising "comparing a database of mRNA sequences" and "determining if, in addition to the target mRNA sequence, one or more additional mRNA sequences in the database are complementary to an 11 consecutive nucleotide sequence of the siRNA nucleotide sequence", wherein "an siRNA nucleotide sequence that consists of 18-25 nucleotides". Such method steps are not described by

page 7 or Figure 4 of 60/513,489. See *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 41 USPQ2d 1961 (Fed. Cir. 1997), wherein the court held at page 1966: “While the meaning of terms, phrases, or diagrams in a disclosure is to be explained or interpreted from the vantage point of one skilled in the art, *all the limitations* must appear in the specification. The question is *not* whether a claimed invention is *an obvious variant* of that which is disclosed in the specification. Rather, *a prior application itself must describe an invention, and do so in sufficient detail* that one skilled in the art can clearly conclude that the inventor invented the claimed invention as of the filing date sought.” (emphasis added). Since applicant’s arguments are not persuasive, the priority denial is maintained.

#### ***Claim Rejections - 35 USC § 102***

Claims 1-5, 10, 13, 48-50, and 52 remain rejected under 35 U.S.C. 102(e) as being anticipated by Liu et al. for the reasons of record as set forth in the Office action mailed on November 13, 2009 and for the reasons stated below.

Applicant's arguments filed on April 13, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are not anticipated because the priority date of the Lie et al. reference is two days after the effective filing date of the instant application. Contrary to applicant’s argument, the effective filing date for claims 1-5, 10, 13, 48-50, and 52 remains as the filing date of the PCT/US04/35124 application, which was filed on October 22, 2004. As such, the Liu et al. reference qualifies as proper 102(e) prior art.

Applicant argues that the claims are not anticipated even if the Liu et al. reference is available as prior art because it fails to teach every element of the claims such that it does not

teach the step of “comparing or identifying at least 11 consecutive nucleotides complementary to the target mRNA sequence including the nucleotide that is third from an siRNA nucleotide sequence’s 5’ end.”, and therefore applicant asserts that the siRNA identification method of Liu et al. is “completely different” from the method claimed in the instant case. Contrary to applicant’s argument, Liu et al. taught every element of the method steps claimed in the instant case as stated in the last Office action. Before addressing the Liu et al. reference, it appears necessary to point out that the term “at least” (in “at least 11 consecutive nucleotides”) reads on the entire length of the 19-mer antisense strand sequence of an siRNA. Now, Liu et al. taught an anti-CLPP1 mRNA-specific siRNA identification/selection method, wherein one compares the entire 19-mer (thus, 19 consecutive nucleotides) to other mRNA sequences by accessing NCBI or ENSEMBL and select the 19-mer sequence having a 100% complementarity to the CLPP1 mRNA as the CLPP1-specific siRNA sequence. That is, since all of the target-specific 19 consecutive nucleotides are 100% complementary to the target sequence, the antisense strand sequence of the selected siRNA must inherently have “at least” 11 consecutive nucleotides complementary to the target sequence. Further, since all of the 19 nucleotides of the antisense strand sequence are complementary to the target mRNA sequence, the third nucleotide from the 5’ end of the antisense strand sequence of the siRNA must also inherently be complementary to the nucleotide in the target mRNA sequence. As such, Liu et al. taught every element claimed in the instant case.

Applicant argues that the claims are not anticipated because the instant rejection is based on “comparing the resulting product rather than the method used to identify the product.” Contrary to applicant’s argument, the method “steps” as well as the resulting end product of Liu

et al. anticipate those claimed in the instant case. Again, note that the term "at least" encompasses the entire length of the antisense strand sequence of an siRNA. Liu et al. taught to identify and select a target-specific siRNA sequence by choosing a 19-mer that is 100% identical or homologous only to the intended target sequence by means of performing sequence homology database searches, and thus synthesizing a 19-mer antisense strand sequence that is 100% complementary to selected 19-mer siRNA sequence, that was found to be unique to the intended target sequence via the database search results. Again, the 19 consecutive nucleotides of Liu et al. are within the meaning of the "at least" 11 consecutive nucleotides including the third nucleotide from the 5' end of the siRNA sequence. Hence, not only the method steps but also the resulting product of a uniquely targeting siRNA molecule are taught by Liu et al.

Since applicant's arguments do not show how the language of the claims patentably distinguishes them from the references, this rejection is maintained.

Claims 1-5, 13, and 48-50 remain rejected under 35 U.S.C. 102(b) as being anticipated by Elbashir et al. for the reasons of record as set forth in the Office action mailed on November 13, 2009 and for the reasons stated below.

Applicant's arguments filed on April 13, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are not anticipated because Elbashir et al. fail to disclose each and every element of claims 1-2. Contrary to applicant's argument, the siRNA identification method disclosed in the Elbashir et al. reference meets every single limitation set forth in claims 1-2. Again, as noted above, the claims are not limited to just an 11-mer for target sequence complementarity. Instead, the "at least" limitation recited in the claims encompasses

the entire 19-mer siRNA sequence. As stated in the last Office action, the siRNA sequence selection methodology of Elbashir et al. that compares a potential 19-mer siRNA sequence to other known gene sequences in the BLAST database allows one to select only the potential siRNA sequence that is not targeted by any other known genes, thereby enabling one to select a unique, target-specific siRNA sequence. Hence, the methodology of Elbashir et al. inherently embody an identification/selection method step of comparing the 11 consecutive nucleotide sequence that includes the third nucleotide from the 5' end of the siRNA sequence to known mRNA sequences contained in the BLAST database. As such, Elbashir et al. teach each and every element of claims 1-2.

Applicant further asserts that the claims have been mischaracterized because the "Office fails to take into account that the claims also states that the 11 consecutive nucleotides must also include the 3<sup>rd</sup> nucleotide from 5' end of the sequence." Contrary to applicant's assertion, the claims were correctly interpreted and the instant rejection was properly applied against the claims as evidenced by the fact that the last Office action explicitly states that Elbashir et al. taught that "the entire 19-mer antisense strand sequence is 100% complementary to the mRNA target sequence.", and therefore, the "methods of Elbashir et al. would necessarily ensure that 11 consecutive nucleotides from the 5' end of the antisense strand sequence are complementary only to the target mRNA" (emphasis added). See pages 7-8. As such, the last Office action correctly characterized the claims since the fact that the entire 19-mer siRNA sequence is 100% complementary to the target sequence, wherein the entire 19-mer necessarily includes 11 consecutive nucleotides from the 5' end of the siRNA sequence, which thus logically reflects the



fact that the third nucleotide from the 5' end of the siRNA sequence is necessarily complementary to a nucleotide in the target mRNA sequence.

Since applicant's arguments are not persuasive, this rejection is maintained.

### ***Claim Rejections - 35 USC § 103***

Claims 1-5, 10, 13, 48-50, and 52 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Elbashir et al., Tuschl et al., Martinez et al., and Ureta-Vidal et al. for the reasons of record as set forth in the Office action mailed on November 13, 2009 and for the reasons stated below.

Applicant's arguments filed on April 13, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are not obvious because the combination of the references do not teach all of the limitations claimed in the instant case and restates the arguments addressed to the 102(b) rejection. As stated hereinabove, the teachings of Elbashir et al. teach all of the limitations set forth in claims 1-2, including the limitation that the third nucleotide from the 5' end of the siRNA sequence is complementary to a nucleotide in the target mRNA. See pages 6-7 hereinabove.

Since applicant's arguments are not persuasive, this rejection is maintained.

### ***Conclusion***

No claim is allowed.

This application contains claim 39 drawn to an invention nonelected with traverse in the reply filed on August 6, 2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi (Acting SPE) can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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